be accomplished. It is obvious that the disease is as a rule detected only in its latest stages and that much earlier diagnosis will be required if the current figures of mortality and morbidity are to be greatly improved.[4] In the earlier stages of the disease when the liver is presumably affected chiefly by fatty degeneration and the portal circulation is not greatly restricted, the results of therapy should be excellent.

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REFERENCES

1. Barker, W. H.: The Modern Treatment of Cirrhosis of the Liver, M. Clin., North America (March, 1945), p. 273.
2. Beattie, J., and Marshall, J.: Methionine in the Treatment of Liver Damage, Nature, London, 153:525, 1944.
3. Bollman, J. L.: Personal Communication to the Author.
4. Chapman, C. B., Snell, A. M., and Rowntree, L. G.: Compensated Cirrhosis of the Liver; a Plea for More Intensive Consideration of the Earlier Stages of Disease of the Hepatic Parenchyma, J.A.M.A., 100:1735, 1933.
5. Chapman, C. B., Snell, A. M., and Rowntree, L. G.: Decompensated Portal Cirrhosis; Report of One Hundred and Twelve Cases, J.A.M.A., 97:237, 1931.
6. Connor, C. L.: The Etiology and Pathogenesis of Alcoholic Cirrhosis of the Liver, J.A.M.A., 112:387, 1939.
7. Crafoord, Clarence and Frenckner, Paul: New Surgical Treatment of Varicose Veins of the Oesophagus, Acta Oto-laryng., 27:422, 1939.
8. Fleming, R. G., and Snell, A. M.: Portal Cirrhosis with Ascites: An Analysis of 200 Cases with Special Reference to Prognosis and Treatment, Am. J. Digest. Dis., 9:115, 1942.
9. Gilbert, Christine and Gillman, Joseph: Diet and Disease in the Bantu, Science, n.s. 99:398, 1944.
10. György, Paul and Goldblatt, Harry: Hepatic Injury on a Nutritional Basis in Rats, J. Exper. Med., 70:185, 1939.
11. György, Paul and Goldblatt, Harry: Observations on the Conditions of Dietary Hepatic Injury (Necrosis, Cirrhosis) in Rats, J. Exper. Med., 75:355, 1942.
12. Hardiker, S. W., and Gopal Rao, V. G.: Ascites in Hyderabad (Deccan); Preliminary Note, J. Indiana M. A., 13:1, 1943.
13. Hoffbauer, F. W., Evans, G. T., and Watson, C. J.: Cirrhosis of the Liver: With Particular Reference to Correlation of Composite Liver Function Studies with Liver Biopsy, M. Clin. North America, March, 1945, p. 363.
14. Iversen, Poul and Roholm, Kaj: On Aspiration Biopsy of the Liver, with Remarks on Its Diagnostic Significance, Acta Med. Scandinav., 102:1, 1939.
15. Lord, J. W., Jr., and Andrus, W. D.: Differentiation of Intrahepatic and Extrahepatic Jaundice; Response of the Plasma Prothrombin to Intramuscular Injection of Menadione 2-methyl-1, 4-naphthoquinone) as a Diagnostic Aid, Arch. Int. Med., 68:199, 1941.
16. Mateer, J. G., Baltz, J. I., Marion, D. F., and MacMillan, J. M.: Liver Function Tests. A general evaluation of liver function tests, and an appraisal of the comparative sensitivity and reliability of the newer tests, with particular emphasis on the cephalin-cholesterol flocculation test, the intravenous hippuric acid test and an improved bromsulphalein test with a new normal standard, J.A.M.A., 121:723, 1943.
17. Neal, P. A., and Von Ocetigen, W. F.: Discussion. In: Conference on Liver Injury, 1944, New York, Josiah Macy, Jr. Foundation, 1944.
18. Patek, A. J., Jr.: Discussion. In: Conference on Liver Injury, 1944, New York, Josiah Macy, Jr. Foundation, 1944.
19. Patek, A. J., Jr.: Treatment of Alcoholic Cirrhosis of the Liver with High Vitamin Therapy, Proc. Soc. Exper. Biol. & Med., 37:329, 1937.
20. Patek, A. J., Jr.: Dietary Treatment of Laennec's Cirrhosis with Special Reference to Early Stages of the Disease, Bull. New York Acad. Med., s. 2, 19:498, 1943.
21. Peters, R. A., Thompson, R. H. S., King, A. J., Williams, D. I., and Nicol, C. S.: Sulphur-containing amino-acids and jaundice, Nature, London, 153:773, 1944.
22. Ratnoff, O. D., and Patek, A. J., Jr.: The Natural History of Laennec's Cirrhosis of the Liver; an Analysis of 386 Cases, Medicine, 21:207, 1942.
23. Rich, A. R., and Hamilton, J. D.: Experimental Production of Cirrhosis of Liver by Means of Deficient Diet, Bull. Johns Hopkins Hosp., 66:185, 1940.
24. Snapper, I.: Chinese Lessons to Western Medicine, New York, Interscience Publishers, Inc., 1941, 380 pp.
25. Snell, A. M., and Butt, H. R.: Hepatic Coma: Observations Bearing on Its Nature and Treatment, Tr. A. Am. Physicians, 56:321, 1941.
26. Tripoli, C. J., and Fader, D. E.: Differential Diagnosis of Certain Diseases of the Liver by Means of Punch Biopsy, Am. J. Clin. Path., 11:516, 1941.
27. Wade, L. J.: Recent Advances in the Therapy of Cirrhosis of the Liver, M. Clin. North America, March, 1945, p. 479.
28. Watson, C. J.: Cirrhosis of the Liver: Clinical Aspects with Particular Reference to Liver Function Tests, Am. J. Clin. Path., 14:129, 1944.

# THE STATUS OF THE LIVER AND ITS IMPORTANCE TO THE SURGEON*

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THE status of the liver and its importance to the surgeon constitutes an exhaustive background for discussion. The functionally and histologically disturbed liver is a sensitive criterion of the degree of damage resulting from many extra hepatic pathological states. Many diseases and many agents result in degenerative changes in the liver. With progression of the disease, the hepatitis is also insidiously progressive and results finally in some degree of irrevocable fibrosis.

The liver has remarkable reparative capacities. A single major injury or repeated minor injuries may result in no permanent damage because of this extraordinary power of regeneration. Continuation of these injuries, however, will eventuate in a chronic generalized hepatitis because of a failure of these regenerative processes and a replacement of the functioning parenchyma with connective tissue.

A comparatively small remnant of normally functioning liver parenchyma will compensate for the whole in such a degree that there is no depression in the hepatic sufficiency tests nor is there symptomatic clinical evidence of disturbed function. Practically, then, it becomes incumbent upon the surgeon to recognize that liver damage is almost invariably sequential to certain surgical diseases and that restoration of hepatic function should be attempted before the elective surgery is undertaken.

## TYPES OF LIVER DISEASE

The most common diseases, either actually or potentially surgical, that eventuate in some degree of hepatic parenchymatous destruction are:

(1) The infections.
(2) The benign peptic ulcer.
(3) Extra-hepatic biliary disease.
(4) Thyrotoxaemia.
(5) Gastro-intestinal malignancies.

*Infections.*—Secondary destruction of liver tissue by infection is not limited to primary peritoneal involvement by the infecting agent. The acute appendix typifies the primary involvement with secondary damage to liver parenchyma through the portal route. Even death may occur without evidences of a spreading peritonitis but with demonstrable depression of hepatic physiology and with gross and histological liver damage.

The acute surgical abdomen may be complicated by concomitant but unrelated diseases that are associated with hepatic involvement. Medical officers with troops are concerned primarily with acute phases of such diseases. The civilian surgeon will be particularly concerned later upon discharge of these service men with the more chronic phases with progressive liver deterioration.[1] These diseases include malaria, sporadic and epidemic hepatitis, leptospiral jaundice or Weils disease, schistosomiasis and amoebic hepatitis.

*Duodenitis with Peptic Ulcer.*—Ascending infection from the duodenum through the Ampulla of Vater characterizes the duodenitis associated with peptic ulcer. Here, as in the portal route of conveyance of the infection, parenchymatous destruction is evident and pylephlebitis with concomitant hepatic miliary abscesses is absent.

*Extra-hepatic Biliary Disease.*—Diseases of the extra hepatic biliary tract and particularly gallbladder disease

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originally stimulated the study of liver sufficiency as it was related to surgical practice. Gallbladder disease is essentially a chronic disease.[2] Acute cholecystitis does occur, but it is usually an acute exascerbation in a chronically diseased gallbladder. In the perennial controversy over the respective merits of the delayed versus the immediate surgical treatment of acute cholecystitis, neither protagonist adequately considers the effect of depressed liver function on the mortality and morbidity rate in individual cases. In the absence of the accepted criteria for emergent surgical intervention, hepatic function, as estimated clinically and by laboratory data, dictates more reliably the time of surgical intervention.

*Thyrotoxaemia.*—In thyrotoxicosis, jaundice is clinically evident is about 5 per cent of patients and particularly in the preoperative crisis. Clinical jaundice is evidence of some degree of hepatitis even though our present laboratory tests fail to measure a depression in function. The most progressively restricted hepatic function in thyrotoxicosis is its ability to metabolize and store glycogen. The histological changes in the liver are variously described and are not consistently identical. Three characteristic changes have been described as common to all patients.[3]

1. Diffuse deposition of fat in the parenchymal cells.
2. Central necrosis of the hepatic cords.
3. Periportal connective tissue proliferation.

Since no proof is available that thyroxine is toxic to the individual cell, the hepatic damage is best explained on the basis of chronic anoxia in a liver already showing increased oxygen consumption and glycogen depletion.[4]

The majority of thyrotoxic patients undoubtedly have only minimal hepatic damage. In that recognizable minority with clinical jaundice or other evidences of liver depression, preoperative preparation and postoperative convalescence are more usually complicated and prolonged.

*Gastro-intestinal Malignancies.*—Gastro-intestinal cancer results in a high incidence of fatty infiltration and probably glycogen depletion in the liver.[5] Demonstration of the diminished hepatic function by our present methods is usual in gastro-intestinal malignancy before liver metastasis occurs. Surgical procedures are tedious and prolonged and contribute towards further postoperative depression. These recent studies advance the possibility that "altered hepatic chemical constitution" complicates the risk in gastro-intestinal cancer and that proper preoperative preparation will change hepatic chemistry and increase resistance to hepatotoxins.

In evaluating the liver function tests it must be recognized that any conclusions are altogether relative. A high degree of hepatitis with dysfunction may be present without laboratory evidence in any of the tests. The latent functional activity of liver parenchyma will remarkably compensate for a major loss and there will be no clinical or other evidence of destruction.

The best estimate of functional capacity is obtained from a correlation of laboratory data and clinical findings.

Chemical tests attempt to determine departures from normal in liver metabolism, including bile, protein, carbohydrate, fat and lipid metabolism and the detoxifying and excretory functions of the liver. In recent reports of experimental study,[6] it was concluded that the bromsulfalein test was the most sensitive in detecting damage while a rise in the serum phosphate value was the second most reliable indication. The prothrombin time was less sensitive but demonstrated damage before the intravenous galactose tolerance test. These findings have not been corroborated clinically.

The hypoproteinemia of hepatitis seems to be selective. As chronicity develops, the serum albumen level becomes more depressed.

## COMMENT

The value of the individual liver function test is easily over estimated. However, used in association, more will become depressed as intrinsic damage progresses.

Clinically, in the absence of extra hepatic biliary obstruction, jaundice is evidence of some degree of degeneration and with further deterioration, renal changes become apparent. Latent hepatic disease, with the contributing and evident extra hepatic lesion, probably accounts for the hepatorenal syndrome and the so called liver death.[7,8] Exploratory evidence of the degree of liver damage is not always reliable in the absence of biopsy.

The details of treatment in depressed hepatic function are not within the province of this discussion. It has long been known that a high fat diet is contra-indicated in the presence of a damaged liver. It has been known, further, that high carbohydrate intake is salutory. These clinical observations have been correlated with the results of experimental investigation. A high concentration of lipid in the liver is pathological, an adequate quantity of stored glycogen is protective but only in the absence of an abnormal content of liver fat.[5]

A high protein intake is clinically beneficial in hepatitis. Recent studies of liver biopsies in surgical patients have furnished a background for this conclusion.[9] A diet high in protein diminishes the deposition of fat in the parenchymal cells and minimizes hepatic destruction. Experimental studies have demonstrated that certain constituents of protein are more effective than the whole protein. Among these components, choline has been used more extensively both experimentally and clinically and there seems to be good reason for its continued use in diseases associated with liver destruction.[10] There are now commercially available protein hydrolysate products. Our clinical experience has been with Amigen. Amigen is a pancreatic hydrolysate of casein and given slowly in dextrose solution, untoward reactions will be minimized and it is well tolerated.

In addition to high carbohydrate, high protein and low fat intake, preparation must include supplementary vitamins, particularly Vitamin B, and adequate Vitamin K administration.

## SUMMARY

Hepatitis with parenchymatous damage is a complicating sequence of many extra hepatic surgical diseases. Latent functional hepatic activity will remarkably compensate for even a major injury and there will be no clinical or other evidences of destruction. Even in the absence of such evidences, some degree of liver damage must be assumed and appropriately treated.

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## REFERENCES

1. Greene, Carl H.: Arch. Int. Med., 73:349 (April), 1944.
2. Johnson, Wm. Malstrom, B. E., Volk, B. W.: Ann. Int. Med., 21:431 (Sept.), 1944.
3. Lord, Jr., J. W., and Andrus, W. D.: Arch. Surg., 42:643, 1941.
4. Buxton, R. W.: Surgery, 16:748 (Nov.), 1944.
5. Ariel, Abels, Murphy, Pack, Rhoads: Ann. Int. Med., 20:570 (April), 1944.
6. Drill, V. A., Ivy, A. C.: J. Clin. Inv., 23:209 (March), 1944.
7. Wilensky, A. O.: Arch. Surgery, 38:625 (April), 1939.
8. Wilensky, A. O.: N. Y. State J. Med., 44:1115 (May 15), 1944.
9. Ravdin, Thorogood, Riegel, Peters, Rhoads: J.A.M.A., 121:322, 1943.
10. Rusakoff, A. H., and Blumberg, Harold: Ann. Int. Med., 21:848 (Nov.), 1944.